

Comparison of 3 Indices for Assessing the Severity of Bronchial Asthma Exacerbations in Children

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Background: The modified pulmonary index score (mPIS) is reported to be useful for assessing bronchial asthma severity. However, mPIS has not been compared with other scores to date. In this study, we have compared mPIS with other scores and clarified the usefulness of mPIS.

Materials and Methods: The study assessed children ($n=67$; median age=3 years) hospitalized for acute exacerbation of bronchial asthma without pneumonia between April 2016 and August 2017. We evaluated mPIS, pulmonary index score (PIS), and modified Wood's Clinical Asthma Score (mWCAS) from their medical record at admission, and we retrospectively evaluated the correlation between each score and clinical outcomes.

Results: The median values for mPIS, PIS, and mWCAS were 9, 7, and 3, respectively. The median durations of hospitalization and of systemic glucocorticosteroid therapy were 7 and 4 days, respectively; 27 patients (40.2%) received continuous inhalation therapy with isoproterenol. All the scores were moderately positively correlated with the duration of hospitalization as follows: mPIS, 0.566 ($P<0.001$); PIS, 0.488 ($P<0.001$); and mWCAS, 0.411 ($P<0.001$). Moderate positive correlations were observed between all scores and the duration of systemic glucocorticosteroid therapy as follows: mPIS, 0.488 ($P<0.001$); PIS, 0.407 ($P<0.001$); and mWCAS, 0.367 ($P=0.002$). Receiver operating characteristic curve analysis of need for continuous inhalation therapy with isoproterenol yielded areas under the curve of 0.91, 0.83, and 0.87 for mPIS, PIS, and mWCAS, respectively.

Conclusions: Correlation of mPIS and outcome was equal to or stronger than that of PIS or mWCAS, and mPIS can be useful for assessing the severity of acute exacerbations of bronchial asthma and predicting prognosis.

Keywords: bronchial asthma, childhood asthma, inhalation therapy, isoproterenol, pulmonary index score

Introduction

BRONCHIAL ASTHMA IS one of the major respiratory diseases requiring hospitalization in children. In Japan, the Japanese Pediatric Guidelines for the Treatment and Management of Asthma 2012 (JPGL 2012)¹ and 2017² are used; the guidelines state that appropriate severity assessment and immediate treatment of acute exacerbations (acute asthma attack), as well as long-term follow-up management, are required.

According to these guidelines, the severity at the time of acute exacerbations is classified into 4 stages, namely mild, moderate, and severe exacerbations, and respiratory failure; and it is judged based on the degree of impairment of the respiratory status and activities of daily living such as eating, speaking, sleeping, and exercising. These 4 stages can easily be distinguished, but in-depth severity cannot be assessed, and it is difficult to evaluate subtle changes in se-

verity over time. The pulmonary index score (PIS, in 1984)³ and Wood's Clinical Asthma Score (WCAS, in 1972)⁴ have long been used for severity assessment of bronchial asthma attacks in many clinical studies. These scores are used to assess the severity of acute exacerbation of asthma.

The PIS evaluates 4 parameters, namely accessory muscle use, inspiratory–expiratory ratio, wheezing, and respiratory rate, each on a scale of 0–3 points (a total of 0–12 points). Similarly, the WCAS evaluates 5 parameters, namely partial pressure of arterial oxygen (PaO_2), inspiratory breath sounds, accessory muscles, expiratory wheezing, and cerebral function, each on a scale of 0–2 points (a total of 0–10 points). Recently, the modified PIS (mPIS) has been reported,⁵ in which parameters of the inspiratory–expiratory ratio of PIS have been simplified, and peripheral capillary oxygen saturation (SpO_2) and heart rate have been added. A total of 6 items are evaluated, each on a scale of 0–3 points (a total of 0–18 points).⁵ In addition, many scoring

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modifications have been made to the WCAS, such as replacing PO_2 with SpO_2 , and changing numerous other parameters.^{6–10} Recent reports have supported the usefulness of mPIS, and it has been shown that mPIS at hospital admission correlates with the duration of hospitalization, treatment, and persistent inhalation of beta stimulants.^{5,11,12}

However, to date, no report has compared the usefulness of mPIS and other scores. This study aimed at clarifying the usefulness of the severity score for acute exacerbation of bronchial asthma by retrospectively evaluating the correlation between the score for each child hospitalized for acute exacerbation of bronchial asthma and outcomes, such as duration of hospitalization.

Materials and Methods

Subjects

In this study, we retrospectively evaluated children ($n=96$) hospitalized at the Saitama Medical Center, Jichi Medical University, for acute exacerbation of bronchial asthma between April 2016 and August 2017. Patients with complications of pneumonia ($n=29$), which could affect the symptom course, were excluded, resulting in the inclusion of 67 patients (Fig. 1).

This study was approved by the Ethics Review Board of Saitama Medical Center, Jichi Medical University (approval no. S17-151) and the need for obtaining informed consent was waived given the retrospective design of this study.

Evaluation of severity at hospitalization

Children with acute exacerbation of bronchial asthma were treated with an inhaled short-acting beta-2 agonist as outpatients and were hospitalized if the treatment effect was insufficient. In our hospital, when a patient is hospitalized with acute exacerbation of bronchial asthma, a pediatrician describes detailed information on vital signs, severity of wheezing and accessory muscle use, breath sounds, inspiratory–expiratory ratio, and level of consciousness, in the patient's medical record according to the format. We, therefore, evaluated the mPIS, PIS, modified WCAS (mWCAS), and intensity of asthma exacerbation, according to JPGL 2012, based on the physical findings and vital signs at hospitalization that were described in the medical records.

In this study, mPIS was evaluated based on 6 parameters, namely SpO_2 , accessory muscle use, inspiratory–expiratory ratio, wheezing, heart rate, and respiratory rate, each on a scale of 0–3 points, and then the total sum (0–18 points). PIS was evaluated as previously described. For mWCAS, we used Ream's mWCAS,⁶ which is similar to the original WCAS (except that PO_2 is replaced with SpO_2). mWCAS was based on 5 parameters, namely SpO_2 , inspiratory breath sounds, accessory muscle use, expiratory wheezing, and cerebral function, each evaluated on a scale of 0–2 points, to obtain a total score (0–10 points) (Table 1). The intensity of asthma exacerbation, according to JPGL 2012, was evaluated in 4 stages: mild, moderate, and severe exacerbations, and respiratory failure.¹

Evaluation of outcomes

Treatment was administered according to JPGL 2012.¹ To evaluate patient outcomes, we assessed the duration of hospitalization, systemic glucocorticosteroid therapy, and presence or absence of continuous inhalation therapy with isoproterenol.

Statistical analysis

We retrospectively evaluated the patients' clinical characteristics, scores, and outcomes, and the results were expressed as the median and interquartile range (IQR). The correlation between each score (mPIS, PIS, mWCAS) at hospitalization and outcomes (duration of hospitalization, duration of systemic glucocorticosteroid therapy) were evaluated by using Spearman's correlation coefficient. P values <0.05 were considered significant. Receiver operating characteristic (ROC) curves were generated to determine the indication of continuous inhalation therapy with isoproterenol for each score. Performance of the model was assessed by using the area under the curve (AUC). Specificity and sensitivity were calculated for the optimal cutoff score. All statistical analyses were performed by using EZR 1.10 software (Saitama Medical Center, Jichi Medical University, Saitama, Japan).¹³

Results

Baseline subject characteristics

Table 2 summarizes the patient characteristics. The median age for all patients was 3.0 years (IQR 2.7–5.2 years), and 73% of the patients were male. Based on JPGL 2012, the severity of asthma was classified as intermittent, mildly persistent, moderately persistent, and severely persistent in 23, 10, 8, and 10 patients, respectively; whereas 16 patients were experiencing their first asthma attack. The long-term drug management consisted of a leukotriene receptor antagonist, an inhaled corticosteroid, and an inhaled salmeterol/fluticasone combination, for 27, 16, and 1 patient, respectively. Twenty-three patients were not on long-term drug management.

Severity scores and the duration of hospitalization and treatment

The median (IQR) score of all hospitalized patients for mPIS, PIS, and mWCAS was 9 (7.5–10.5), 7 (5–8), and 3

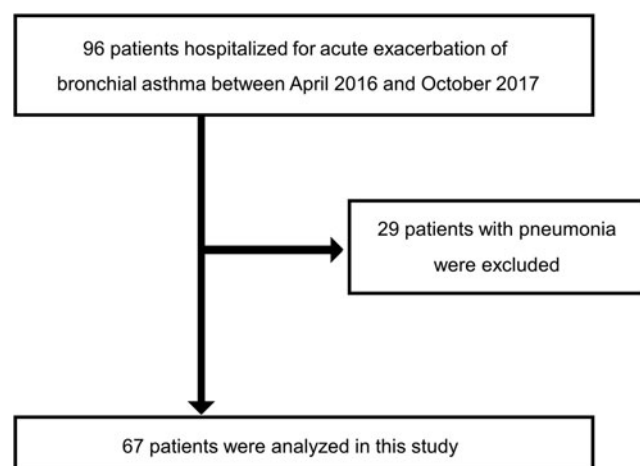


FIG. 1. Study enrollment scheme.

TABLE 1. CHARACTERISTICS OF THE SCORES

	Score			
	0	1	2	3
<i>Pulmonary index score</i>				
Accessory muscle use	0	+/-	++	+++
Inspiratory–expiratory ratio	5:2	5:3–5:4	1:1	<1:1
Wheezing	None	Terminal expiration, with stethoscope	Entire expiration, with stethoscope	Inspiration and expiration, without stethoscope
Respiratory rate/min	≤30	31–45	46–60	<60
<i>Modified pulmonary index score</i>				
	0	1	2	3
Oxygen saturation % (room air)	≥96	93–95	90–92	<90
Accessory muscle use	None	Mild	Moderate	Severe
Inhalation–exhalation ratio	1:1	1:1	1:2	1:3
Wheezing	None	End expiratory	Inspiratory and expiratory wheeze, good aeration	Inspiratory and expiratory wheeze, decreased aeration
Heart rate/min				
<3 years old	<120	120–140	141–160	≥160
≥3 years old	<100	100–120	121–140	≥140
Respiratory rate/min				
<6 years old	<30	31–45	46–60	≥60
≥6 years old	<20	21–35	36–50	≥50
<i>Modified Wood's clinical asthma score</i>				
	0	1	2	
Oxygenation SpO ₂ %	95–100 (in air)	≤94 (in air)	≤94 (in 40% FiO ₂)	
Inspiratory breath sounds	None	Unequal	Decreased or absent	
Accessory muscle use	Normal	Moderate	Maximal	
Expiratory wheezing	None	Moderate	Marked	
Cerebral function	Normal	Depressed/agitated	Coma	

(2–5), respectively. The median (IQR) of the duration of hospitalization and the duration of systemic glucocorticosteroid therapy was 7 (6–8.5) days and 4 (3–5) days, respectively. In addition, 27 patients received continuous inhalation therapy with isoproterenol (Table 3).

Correlation between each score and outcomes. We found moderate, positive correlations between all scores and the duration of hospitalization, as follows: mPIS, 0.566 ($P < 0.001$); PIS, 0.488 ($P < 0.001$); and mWCAS, 0.411 ($P < 0.001$) (Fig. 2). Similarly, there were moderate, positive

TABLE 2. PATIENT CHARACTERISTICS

Characteristics	Total (n = 67)
Sex, male:female	49:18
Median age (years)	3.0 (2.7–5.2)
Classification of asthma severity by JPGL 2012	
Intermittent	23 (34.3%)
Mild persistent	10 (14.9%)
Moderate persistent	8 (11.9%)
Severe persistent	10 (14.9%)
First attack	16 (23.8%)
Long-term management drugs (controllers)	
LTRA	27 (40.2%)
ICS (low dose)	3 (4.4%)
ICS (medium dose)	3 (4.4%)
ICS (high dose)	10 (14.9%)
SFC	1 (1.4%)

Data are presented as medians (with IQR: 25–75 percentiles) or n (%).

ICS, inhaled corticosteroid; IQR, interquartile range; JPGL 2012, Japanese Pediatric Guidelines for the Treatment and Management of Asthma 2012; LTRA, leukotriene receptor antagonist; SFC, salmeterol/fluticasone combination drug.

TABLE 3. EVALUATION OF SEVERITY AND OUTCOME

Evaluation of severity	
Severity of asthma exacerbation by JPGL 2012	
Mild	3 (4.4%)
Moderate	44 (65.7%)
Severe	20 (29.9%)
Respiratory failure	0 (0%)
Modified pulmonary index score	9 (7.5–10.5)
Pulmonary index score	7 (5–8)
Modified Wood's clinical asthma score	3 (2–5)
Outcome	
Duration of hospitalization (days)	7 (6–8.5)
Treatment	
Continuous inhalation therapy with isoproterenol	27 (40.2%)
Duration of systemic glucocorticosteroid therapy (days)	4 (3–5)

Data are presented as medians (with IQR: 25–75 percentiles) or n (%).

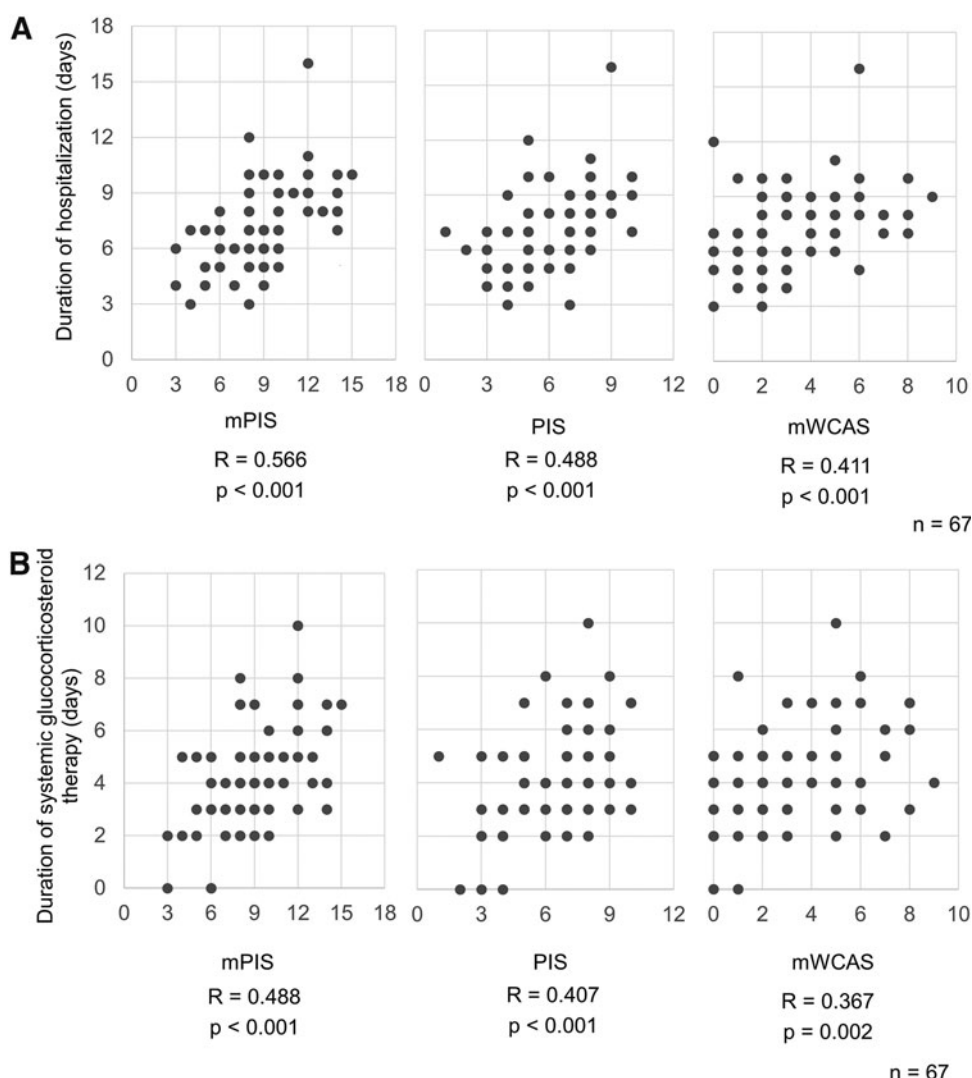


FIG. 2. (A) Correlation between each score and the duration of hospitalization. (B) Correlation between each score and the duration of systemic glucocorticosteroid therapy.

correlations between all scores and the duration of systemic glucocorticosteroid therapy, as follows: mPIS, 0.488 ($P < 0.001$); PIS, 0.407 ($P < 0.001$); and mWCAS, 0.367 ($P = 0.002$) (Fig. 3).

ROC curve analysis. In ROC curve analysis for determining the indication for continuous inhalation therapy with isoproterenol, the AUCs of mPIS, PIS, and mWCAS were 0.91 [95% confidence interval (CI) 0.849–0.975], 0.83 (95% CI 0.745–0.932), and 0.87 (95% CI 0.785–0.956), respectively. The AUC of mPIS was higher than that of PIS or mWCAS. For mPIS, with 10 as the optimal cutoff value (according to the Youden index), we obtained specificity and sensitivity values of 74.1% and 87.5%, respectively. For PIS at an optimal cutoff of 7 (according to the Youden index), we obtained specificity and sensitivity values of 81.5% and 70%, respectively. For mWCAS, with an optimal cutoff of 4 based on the Youden index, specificity and sensitivity values were 85% and 70.3%, respectively.

Discussion

In recent times, the control of bronchial asthma has improved due to the more widespread use of management medication, such as inhaled steroids, and the proportion of hospitalized patients who are severely affected has been

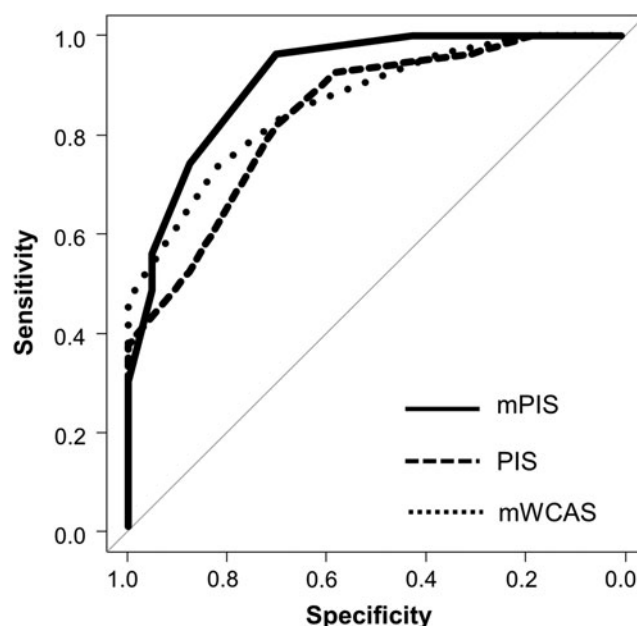


FIG. 3. ROC curve analysis for determining the indication of continuous inhalation therapy with isoproterenol. ROC, receiver operating characteristic.

decreasing. Therefore, a scoring method suitable for evaluating the symptoms of patients with mild-to-moderate bronchial asthma acute exacerbations is necessary. In this study, we investigated the severity score for acute exacerbation in bronchial asthma, treatment, and hospitalization period, and we examined the usefulness of mPIS, PIS, and mWCAS. All the scores correlated with the patient outcomes, demonstrating their usefulness; correlation of mPIS and outcome was equal or stronger than that of PIS or mWCAS.

Previous studies have reported the correlation between mPIS and the duration of treatment and hospitalization. Carroll et al.⁵ reported a correlation between mPIS and the continuous albuterol inhalation period ($R=0.76$, $P<0.001$), duration of oxygen inhalation ($R=0.70$, $P=0.002$), and duration of hospitalization ($R=0.70$, $P=0.04$). In the ROC curve analysis for the indication of intensive care unit hospitalization, the AUC of mPIS at hospitalization was 0.82 (sensitivity of 88% and specificity of 91%, at a cutoff value of 12 points).⁵ Buyukiryaki et al.¹¹ reported a correlation between mPIS during outpatient visits and the hospitalization indication (sensitivity of 45%, and specificity of 79%, at an mPIS cutoff value of 7 points). Similarly, there was a correlation between mPIS after 1 h of outpatient treatment and an indication for hospitalization (sensitivity of 42%, specificity of 85%, at a cutoff value of 5 points).¹¹ Koga et al.¹² reported that there was a correlation between mPIS and the duration of hospitalization ($R=0.34$, $P<0.01$ in all cases, $R=0.57$, $P<0.01$ in the case of continuous inhalation therapy). In the ROC curve analysis for the indication of continuous inhalation therapy during hospitalization, the sensitivity was 74% and the specificity was 74% at an mPIS cutoff value of 12.¹² Similarly, in our study, there was a correlation between mPIS and the duration of hospitalization ($R=0.566$, $P<0.001$) and the duration of systemic glucocorticosteroid therapy ($R=0.488$, $P<0.001$); whereas the ROC curve analysis to determine the indication for continuous isoproterenol inhalation therapy yielded an AUC of 0.912 (sensitivity of 87%, specificity of 74%, at an mPIS cutoff point of 10 points).

The probable reason that our research demonstrated equivalent or higher correlation than past reports could be that this study excluded cases with complications of pneumonia, allowing accurate determination of the severity of respiratory disorder due only to bronchial asthma.

WCAS is the severity score of bronchial asthma acute exacerbation reported by Wood et al.⁴ in 1972. There was a positive correlation between WCAS and PaCO_2 ($R=0.69$, $P<0.001$) and a negative correlation between WCAS and PO_2 ($R=0.44$, $P<0.05$).⁴ mWCAS has been used in many studies, and since each item is classified into only 3 stages (0–2 points), most cases of mild or moderate severity have a total of 0–1 point, and it may be difficult to evaluate the severity in cases with mild or moderate severity in detail. In fact, in our study, 16 out of 67 cases (23%) scored 0–1 point (mWCAS), and the range of duration of hospitalization in cases with 0 points was as wide as 3–12 days (Fig. 2). For mPIS, no case had 0 points, patient scores were dispersed over a range of 3 to 15 points (maximum 18 points), and there was a tendency for the correlation with the duration of hospitalization and systemic glucocorticosteroid therapy to be stronger than those with the other scores. In addition, the 2 additional evaluation categories in mPIS than in PIS may have contributed to the stronger correlation.

Our study had several limitations; the first is that the same doctor did not evaluate the physical findings and vital signs for all patients. However, for mPIS, it has previously been reported that there were fewer scoring differences between evaluators.^{12,14} Second, the age of the target patients in our study was low. Due to the spread of bronchial asthma control drugs, such as inhaled steroids, the number of hospitalized older children with bronchial asthma has decreased, and the median age of the subjects in our study was 3 years (IQR 2.7–5.2 years). Third, the generalizability of the findings is limited because our study is a single-center clinical trial. Therefore, the severity of bronchial asthma patients and the treatment may not be representative of the entire patient population. For example, in this study, there were no patients with respiratory failure. In addition, if the conditions for approving discharge are different in different hospitals, the hospitalization period will vary; hence, the usefulness of the scores may change. Although this study clarified the tendency of usefulness of each score, it is necessary to conduct a large-scale survey of a wide range of severity in the patients, including acute respiratory failure.

To investigate whether similar results can be obtained with pediatric patients of all ages, future research in older children is necessary.

Conclusion

In conclusion, the mPIS, PIS, and mWCAS at admission for children hospitalized with bronchial asthma all correlated with the duration of hospitalization and systemic glucocorticosteroid therapy, and indication for continuous inhalation therapy with isoproterenol; correlation of mPIS and outcome was equal to or stronger than that of PIS or mWCAS. mPIS can be considered useful for assessing the severity of acute exacerbations in bronchial asthma and for predicting prognosis.

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Ethical Approval

This study was approved by the Ethics Review Board of Saitama Medical Center, Jichi Medical University (approval no. S17-151), and the need for obtaining informed consent was waived given the retrospective design of this study.

Authors' Contributions

E.M. wrote the article. E.M., K.I., S.K., Y.S., D.S., K.N., and Y.H. contributed to data collection and analysis. K.I. advised on study design and helped to draft the article. All authors read and approved the final article.

Author Disclosure Statement

No competing financial interests exist.

References

1. Hamasaki Y, Kohno Y, Ebisawa M, et al.; Japanese Society of Pediatric Allergy and Clinical Immunology. Japanese Pediatric Guideline for the Treatment and Management of Asthma 2012. Tokyo: Kyowa Kikaku, 2012.
2. Arakawa H, Hamasaki Y, Kohno Y, et al. Allergology International Japanese Guidelines for Childhood Asthma 2017. *Allergol Int* 2017; 66:190–204.
3. Becker AB, Nelson NA, Simons FE. The pulmonary index. Assessment of a clinical score for asthma. *Am J Dis Child* 1984; 138:574–576.
4. Wood DW, Downes JJ, Lecks HI. A clinical scoring system for the diagnosis of respiratory failure. Preliminary report on childhood status asthmaticus. *Am J Dis Child* 1972; 123: 227–228.
5. Carroll CL, Sekaran AK, Lerer TJ, et al. A modified pulmonary index score with predictive value for pediatric asthma exacerbations. *Ann Allergy Asthma Immunol* 2005; 94:355–359.
6. Ream RS, Loftis LL, Albers GM, et al. Efficacy of IV theophylline in children with severe status asthmaticus. *Chest* 2001; 119:1480–1488.
7. Parkin PC, Macarthur C, Saunders NR, et al. Development of a clinical asthma score for use in hospitalized children between 1 and 5 years of age. *J Clin Epidemiol* 1996; 49:821–825.
8. Kim IK. Helium-oxygen therapy for infants with bronchiolitis. *Arch Pediatr Adolesc Med* 2011; 165:1115–1122.
9. Liet JM, Ducruet T, Gupta V, et al. Heliox inhalation therapy for bronchiolitis in infants. *Cochrane Database Syst Rev* 2015; 9:CD006915.
10. Chowdhury MM, McKenzie SA, Pearson CC, et al. Heliox therapy in bronchiolitis: Phase III multicenter double-blind randomized controlled trial. *Pediatrics* 2013; 131:661–669.
11. Buyuktiryaki AB, Civelek E, Can D, et al. Predicting hospitalization in children with acute asthma. *J Emerg Med* 2013; 44:919–927.
12. Koga T, Tokuyama K, Itano A, et al. Usefulness of modified pulmonary index score (mPIS) as a quantitative tool for the evaluation of severe acute exacerbation in asthmatic children. *Allergol Int* 2015; 64:139–144.
13. Kanda Y. Investigation of the freely available easy-to-use software 'EZ' for medical statistics. *Bone Marrow Transplant* 2013; 48:452e8.
14. Maekawa T, Oba MS, Katsunuma T, et al. Modified pulmonary index score was sufficiently reliable to assess the severity of acute asthma exacerbations in children. *Allergol Int* 2014; 63:603–607.

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